Original Article

A randomised prospective comparison of equilibration point and changing gas composition during low-flow anaesthesia with sevoflurane vs desflurane

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ABSTRACT

Background and Aims: Safety and economy are the main concerns while using low- flow anaesthesia with newer inhalational agents. The main objective of this study was to use and compare 'equilibration time' of sevoflurane and desflurane after change-over from high-to-low flow anaesthesia. **Methods:** This prospective study included consenting adult patients between 18–70 years undergoing elective surgery under general anaesthesia. Patients were randomised initially to receive high-flow anaesthesia with 1.3 MAC of either desflurane or sevoflurane with nitrous oxide. After equilibration point, low-flow anaesthesia was initiated. Heart rate, non-invasive blood pressure, pulse oximeter, 5 electrode ECG and gas monitoring was done. Statistical analysis was done with the help of Med CalC version 12.5.0.0 (student version) and IBM SPSS Version 20.0. **Results:** Mean equilibration time in sevoflurane group was higher (4.59 ± 0.77 minutes) than desflurane group (3.78 ± 0.56 minutes, $P < 0.001$). Inspired concentrations of both inhalational agents varied from their vaporiser settings over 2 hours, more so with sevoflurane than desflurane. Inspired oxygen concentration (FiO2) remained above 30% during anaesthesia in both groups with stable haemodynamics. **Conclusion:** Change-over from high-to-low flow anaesthesia is faster in desflurane. With fresh gas flow (FGF) of 1 L with 50% oxygen and dial concentration of 1–1.5% of sevoflurane and 3.8–4.4% of desflurane, the risk of hypoxia is minimal. The disparity between the set and delivered concentrations is more (20%) in sevoflurane than desflurane (12%).

Key words: Desflurane, low-flow anaesthesia, sevoflurane

INTRODUCTION

There is increasing interest in low-flow anaesthesia (LFA) in clinical practice because of its obvious advantages such as a reduction in the cost of expensive agents like desflurane and sevoflurane and prevention of environmental pollution. Availability of better monitoring devices and newer agents with low blood/gas solubility has facilitated a reduction in the fresh gas flow (FGF) after the initial 'wash-in' period. Various techniques and endpoints are in use to shift from high-flow to low-flow anaesthesia. One of the techniques includes giving high FGF of 6–10 L/min initially for about 3–6 min to reach a high level of alveolar gas concentration to achieve surgical anaesthesia (loading) which is followed by a reduction in total gas flows during maintenance.[1] An alternative technique is using low FGF from the beginning with very high vaporiser setting to achieve target alveolar concentration.[2] Haemodynamic stability during this phase may be a challenge.

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Another challenge during LFA is changing gas composition which often creates a discrepancy between the set concentration and actual inspired concentration of gases delivered by the machine. Under-delivery of agents at very low flow rates is a known phenomenon. In addition, nitrous oxide (N_2O), when used as a component of carrier gas may increase the risk of delivering a hypoxic mixture. The economy of gases is as important as safety and predictability of anaesthesia. The main objective of this study was to use and compare 'equilibration time' of sevoflurane and desflurane as an endpoint to switch to LFA with 1 L of FGF along with N_2O. 'equilibration time' of the agent is defined as the time when the ratio of concentration of expired to inspired agent (Fe/Fi) reaches 80%.[3]

A secondary objective was to monitor changing gas composition in the circuit to detect hypoxia and the haemodynamic parameters during induction and maintenance of anaesthesia.

METHODS

The study included male and female patients between 18–70 years, American Society of Anesthesiology Physical Status I and II (ASA PS) who underwent elective surgery of approximate duration of 2 hours under general anaesthesia. Patients having cardiac and respiratory disease, pregnancy, anaemia or those undergoing laparoscopic surgery were excluded. All study procedures were carried out in conformity with the provisions of the Declaration of Helsinki 2013. The study was carried out between Janaury and December 2017.

After taking approval from the Institutional Ethics Committee, (Date-17/09/2014, BARC Medical Ethics Committee, BHMEC/DNB/24/2014) 60 consecutive patients who fulfilled inclusion criteria were randomised using sealed-envelope technique based on computer-generated random numbers into two groups, group D (Desflurane, 30 patients) and group S (Sevoflurane, 30 patients). After a written and informed consent, they were given oral ranitidine 150 mg and oral alprazolam 0.5 mg on the previous night and were fasting 8 hours prior surgery. After arriving at the operating room, an intravenous line was established and Ringer's lactate solution was started through a fluid warming device at 40°C. A Drager Primus workstation was used for anaesthetics delivery and a well-calibrated 'Infinity Kappa' was used for monitoring. Drager *Vapor* 2000 and D-*Vapor* were used as a sevoflurane and desflurane vaporisers, respectively. Baseline monitoring included an electrocardiogram (ECG), heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SpO_2), end-tidal CO_2 ($EtCO_2$) and gas monitoring.

All patients were pre-oxygenated with 100% oxygen (O_2) at 6 L/min for 3 min. Both groups of patients received intravenous (IV) fentanyl 2 μg/kg and propofol 2–3 mg/kg followed by IV vecuronium bromide 0.1 mg/kg. The trachea was intubated under direct laryngoscopy with the appropriate size of the endotracheal tube, and intermittent positive pressure ventilation started with a tidal volume of 7 ml/kg, rate of 12/min with O_2 and N_2O in a ratio 40:60 with an FGF of 6 L/min. Inhalational agent, desflurane in group D and sevoflurane in group S, was given by gradually increasing the dial concentration by 1% every 3 min to reach 1.3 minimum alveolar concentration (MAC) age-specific value.[4] This can be obtained by matching the corresponding value of 1.3 MAC of a given inhalational agent with the age of patient as given in the graph by Nickalls *et al*.[4] The inspired and expired gas concentrations were monitored every min for the first 5 min. The point of time when the ratio of the concentration of expiratory: inspiratory inhalation agent became 0.8 (equilibration time) was used as a switch-over point for LFA. Total gas flows were reduced to 1 L/min with 50% N_2O. Intra-operatively, age-specific 1 MAC of inhalational agent was maintained by adjusting dial flow concentration to obtain end expired inhalational agent concentration corresponding to the age-specific value shown in the MAC graph without altering the total gas flow.[4] In case inspired O_2 concentration fell to <40%, it was corrected by increasing O_2 in FGF from 50% to 55%. HR, NIBP, SpO_2, $EtCO_2$, inspiratory and expiratory concentrations (Fi and Et) of O_2, N_2O, sevoflurane or desflurane were monitored every minute for first 5 mins followed by every 5 mins for 30 mins and thereafter every 15 mins till the end of surgery. The intermittent top-up dose of vecuronium 0.25 mg/kg was given as indicated till 1 hour before the estimated end of surgery. Fentanyl 0.5 μg/kg increments were given to all patients before the incision and repeated thereafter every hour.

At the end of surgery (completion of last skin stitch), the inhalational agent was switched off. The residual neuromuscular block was reversed with IV neostigmine 50 μg/kg and IV glycopyrrolate 0.01 mg/kg. After

ensuring the adequate rate and depth of respiration nitrous oxide was switched off and only oxygen 6 L/min was given and the trachea was extubated after which patients were asked to open their eyes and follow simple verbal commands and repeat this at an interval of every minute. Wash-out period was taken as the time from the discontinuation of the inhalational agent to the time patient opened his/her eyes on verbal commands. Patients were shifted to the post-anaesthesia care unit (PACU) and observed for about 2 hours. They were asked about any possible recall of intra-operative events before discharge from PACU.

From the previous study by Chatrath *et al*., the equilibration point of sevoflurane was 8.22 (±1.060) min.[5] Power analysis using Cochrane's formula with above SD before the study showed that 25 patients in each of the two groups would allow an 80% chance of detecting a 30% difference in equilibration point of desflurane and sevoflurane in LFA. Expecting a few drop-outs, 30 patients were enrolled in each group.

After data collection, data entry was done in Excel 16.0.6366.2036. Statistical analysis was done with the help of Med CalC version 12.5.0.0(student version) and IBM SPSS Version 20.0. Independent sample students *t*-test was used for parametric studies like equilibration time, wash-out period, inspiratory O_2 (FiO_2), expiratory O_2 (EtO_2), inspiratory N_2O (FiN_2O), end-tidal N_2O (EtN_2O), dial concentration, HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Average values of inspired and expired O_2 and N_2O were plotted graphically on specified time points for comparison between the two groups. *P* value less than 0.05 was taken as a level of significance.

RESULTS

Both groups were comparable as regards to the demographic data [Table 1]. In group S, the average duration of anaesthesia was 131 ± 62 min whereas in group D, it was 114 ± 0.52 min. Group S recorded a mean equilibration time of 4.59 ± 0.77 min while in group D, it was 3.78 ± 0.56 min ($P = 0.00$). In the initial 1st min of starting inhalational anaesthesia, average inspiratory oxygen concentration was significantly lower (47.40% ± 9.26) in group D than in group S (55.60% ± 11.70, $P < 0.001$). The maximum drop in FiO_2 during high-flow anaesthesia was seen at the 4th min which was 43.50% in group S and 38.53% in group D ($P < 0.001$) [Figure 1]. In group S, mean FiN_2O was 31.33% ± 9.75, whereas in group D, it was 37.16% ± 10.08. ($P = 0.02$).

Table 1: Demographic data

Parameter	Group S (Mean±SD)	Group D (Mean±SD)	*P*
Age (yr)	45.53±12.9	44.4±12.3	0.73
Gender	11M/19F	12M/18F	0.99
Weight (kg)	64.3±9.9	62.1±8.0	0.34
Duration of surgery (min)	131±36	114±30	0.06
Equilibration time (min)	4.5±0.7	3.7±0.5	0.00

After switching over to LFA, during maintenance , inspired FiO_2 showed a brief rise for a short period of 10-15 min in both the groups and thereafter gradually declined. During anaesthesia FiO_2 remained above 30% in all the patients of both the groups at all times. FiN_2O and EtN_2O concentration in both groups showed a very steady rise. In both groups it gradually reached a maximum value of 52.67% from 45.96% (group S) and 52% from 45.1% (group D, $P = 0.86$) [Figure 2] which was neither statistically nor clinically significant. Once the equilibration was achieved, average dial concentration to maintain age-specific 1 MAC of inhalational agent ranged between 1.4–1.5% for sevoflurane and 3.8–4.4% for desflurane.

In both groups, haemodynamics were comparable. In group S, the average wash-out period was (11.01 ± 1.33 min) which was significantly higher than average wash-out period in group D (7.63 ± 1.21 min, $P = 0.00$). Average vaporiser setting in group S at 5, 30, 60 and 120 min ranged between 1.55 and 1.44 while in group D, corresponding dial setting ranged between 4.9 and 3.8. [Table 2]. The inspired concentrations of both inhalational agents varied from the vaporiser settings over 2 hours, more so with group S than with group D.

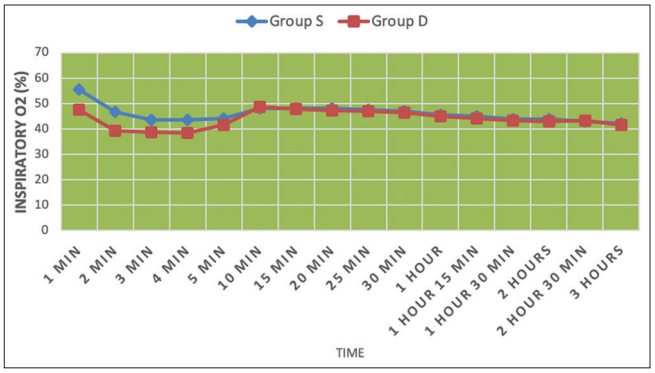

Figure 1: Comparison of inspiratory O_2 at various interval

DISCUSSION

Modern but expensive inhalational anaesthetics such as desflurane and sevoflurane can be used safely and effectively in low-flow technique. We aimed to compare equilibration time, changing the gas composition and haemodynamic changes during LFA with desflurane and sevoflurane. We used 'equilibration time' to change-over from high-to-low flows. During LFA we maintained age-specific 1 MAC of inhalational agent with 50% N_2O as the carrier gas.

Because of lower mean equilibration time found in group D (3.78 min ± 0.56) than group S, we could switch to LFA earlier in group D than in group S. Due to its lowest blood/gas solubility desflurane achieves alveolar concentration faster than sevoflurane. So, the time taken to achieve 80% uptake of the agent by the tissue is less in desflurane compared with sevoflurane. Malik *et al*. compared desflurane and isoflurane in minimal flow anaesthesia.[3] The mean equilibration time obtained for desflurane was 4.96 ± 1.6 min, which is comparable to our observation of 3.78 ± 0.56 min. and also much less than Sathitkarnmanee T *et al*. who used FGF without nitrous oxide[6] Chatrath *et al*. have documented mean equilibration time of 8 min for sevoflurane, which is much more than what we recorded (4.59 ± 0.77 min).[5] They used 2.6% concentration of sevoflurane for all patients while we used age-specific MAC value that

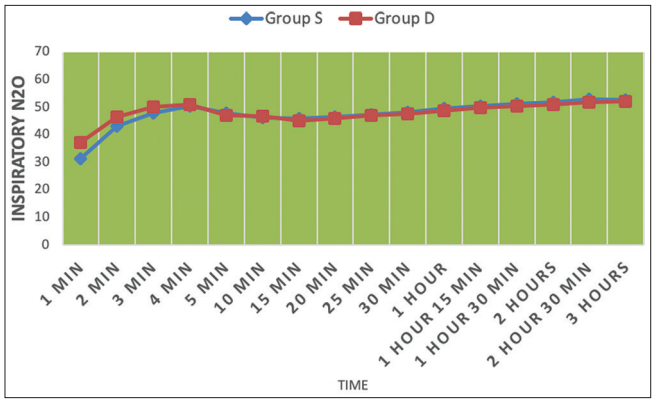

Figure 2: Comparison of inspiratory N_2O at various interval

may have shortened the equilibration time in some cases reducing the average. In the earlier studies, Thepakorn *et al*. have used 1:1:12 wash in the scheme of desflurane using 1 L O_2 and N_2O each and 12% desflurane[2,5] that yielded a shorter wash-in period for desflurane. However, it caused tachycardia and hypotension. Though it was clinically not significant as per the authors, such induction may pose risk to vulnerable patients. Elbert and Muzi observed that increasing the concentration of desflurane from 1.0 to 1.5 MAC resulted in sympathoexcitation in healthy volunteers.[7] In our study, stable heart rate during group D can be attributed to the fact that the desflurane concentration was increased slowly with 1.0% increments every 3 breaths, avoiding over pressurizing. Kapoor and Vakamudi have suggested the same in their review article.[8] IV fentanyl 2 µg/kg helped in attenuating the sympathetic stimulation with desflurane wash-in.[9] In LFA, N_2O usually shows an increasing trend of its concentration while O_2 shows a decreasing trend because the body consumes O_2 and not N_2O.[1] In our study, O_2 was kept at 50% after shifting to LFA. A higher concentration of O_2 compared with conventional technique is recommended in LFA to prevent undesirable fall in FiO_2 especially, while using N_2O.[10] We observed that FiO_2 remained above 30% with an insignificant increase in Fi and Et N_2O in both groups justifying a higher percentage of O_2 in FGF.

We used fentanyl 0.5 µg/kg prior skin incision and every hour intra-operatively to attenuate haemodynamic responses during surgical stimulus.

Inan G, *et al*. have mentioned discrepancy in vaporiser setting and inspired concentration during LFA with and without nitrous oxide.[10] Johansson *et al*. found around 30% reduction in sevoflurane concentration compared to vaporiser setting at 1 L FGF after 120 min which is substantially more than what we recorded.[11] Bozcurt *et al*. also found the discrepancy between the dial concentration and expired / inspired concentrations of inhalational

Table 2: Changing Gas composition

Time	Dial concentration of sevoflurane (Group S)	Inspiratory concentration of sevoflurane	Dial concentration of desflurane (Group D)	Inspiratory concentration of desflurane
5 min	1.55(± 0.15)	1.4(± 0.24)	4.99(±0.37)	4.1(±0.97)
30 min	1.49(± 0.07)	1.17(±0.09)	3.95(±0.74)	3.59(±0.60)
60 min	1.48(± 0.06)	1.18(±0.08)	4.01(±0.67)	3.63(±0.62)
90 min	1.48(± 0.05)	1.17(±0.06)	4.10(± 0.62)	3.7(±0.61)
120 min	1.44(±0.08)	1.15(±0.08)	3.8(±0.55)	3.53(±0.55)

agent. This discrepancy is less during N_2O–O_2 based anaesthetic than with 100% O_2. probably due to second gas effect[12] We observed that the disparity between the set and delivered concentrations is more (20%) in group S than group D (12%).

Recovery from anaesthesia was significantly faster in group D than in group S. The lower partition coefficients of desflurane favour its more rapid elimination from the body.[13] Wash-out period of 7.2 min for desflurane has been mentioned by Ergonenc *et al*. which is comparable to ours.[14] In their randomised prospective double-blind comparison between sevoflurane and desflurane recovery characteristics, longer wash-out and recovery times of sevoflurane were attributed to the residual effect of hexafluoroisopropanol and compound A. Werner JG, *et al*. compared the effect of desflurane and sevoflurane on anaesthesia recovery time. They observed the mean time for eye opening, which was (5.0 ± 2.5 min) for desflurane and (7.9 ± 4.1 min) for sevoflurane, which is lower compared to our observation.[15] The faster wash-out for inhalational agents in their study can be attributed to the lower MAC between 0.5 and 1 used with IV fentanyl and propofol boluses under bispectral index (BIS) monitoring.

Above findings suggest that it is rare to get clinically significant hypoxia at the 50% O_2 and the dial concentration mentioned in the study for maximum 2.5 hours. By 2 hours the delivered concentration is 20% less than the vaporiser setting in sevoflurane and 12% less in desflurane inspite of using flow-compensated and temperature-regulated vaporisers. This is close to what Hendrickx JF *et al*. have reported with 1 L FGF using nitrous oxide after 55 min of anaesthesia[16]

Though we have ensured adequate depth of anaesthesia by keeping age-specific 1 MAC, we have not used any monitor to measure the depth of anaesthesia. Surgeries of longer duration may have further discrepancies during LFA.

CONCLUSION

We conclude that 'equilibration time' of desflurane is significantly lower than that of sevoflurane. With FGF of 1 L with 50% oxygen and dial concentration of 1–1.5% of sevoflurane and 3.8–4.4% of desflurane, the risk of hypoxia is uncommon till 2.5 hours of LFA. However, monitoring FiO_2 is essential. The disparity between the set and delivered concentrations of sevoflurane is more (20%) than desflurane (12%). Users without the facility for agent monitoring should keep this in mind.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Upadya M, Saneesh PJ. Low-flow anaesthesia – underused mode towards "sustainable anaesthesia". Indian J Anaesth 2018;62:166-72.
2. Sathitkarnmanee T, Tribuddharat S, Suttinarakorn C, Nonlhaopol D, Thananun M, Somdee W, *et al*. 1-1-12 one-step wash-in scheme for desflurane-nitrous oxide low-flow anesthesia: Rapid and predictable induction. Biomed Res Int 2014;2014:867504.
3. Mallik T, Aneja S, Tope R, Muralidhar V. A randomized prospective study of desflurane versus isoflurane in minimal flow anesthesia using "equilibration time" as the change-over point to minimal flow. J Anaesthesiol Clin Pharmacol 2012;28:470-5.
4. Nickalls RW, Mapleson WW. Age-related iso-MAC charts for isoflurane, sevoflurane and desflurane in man. Br J Anaesth 2003;91:170-174
5. Chatrath V, Khetarpal R, Bansal D, Kaur H. Sevoflurane in low-flow anaesthesia using "equilibration point". Anesth Essays Res 2016;10:284-90.
6. Sathitkarnmanee T, Tribuddharat S, Nonlhaopol D, Thananun M, Somdee W. 1-1-12 one-step wash-in scheme for desflurane low flow anaesthesia: Performance without nitrous oxide. Drug Des Devel Ther 2015;9:977-81.
7. Eberts TJ, Schmid PG. Inhaled anesthetics. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, editors. Clinical Anesthesia. 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2009. p. 413-43.
8. Kapoor MC, Vakamudi M. Desflurane-revisited. J Anaesth Clin Pharmacol 2012;28:92-100.
9. Hönemann C, Hagemann O, Doll D. Inhalational anaesthesia with low fresh gas flow. Indian J Anaesth 2013;57:345-50.
10. Inan G, Celebi H. A randomized prospective study of BIS guided low-flow sevoflurane anaesthesia; is air safer than nitrous oxide? Anaesth Pain & Intensive Care 2016;20:266-72.
11. Johansson A, Lundberg D, Luttropp HH. The quotient end-tidal/inspired concentration of sevoflurane in a low-flow system. J Clin Anesth 2002;14:267-70.
12. Bozkurt P, Emir NS, Tomatır E, Yeker Y. N2O-free low-flow anaesthesia technique for children. Acta Anaesthesiol Scand 2005;49:1330-3.

13. Srivastava M, Chowdhury I, Bhargava AK. Emergence and recovery characteristics after low flow anaesthesia with desflurane and sevoflurane in cancer patients administered combined epidural and general anaesthesia. Ann Int Med Den Res 2017;3:AN49-53.
14. Ergönenç J, Ergönenç T, İdin K, Uzun U, Dirik A, Gedikli G, *et al*. The recovery time of sevoflurane and desflurane and the effects of anaesthesia on mental and psychomotor functions and pain. Anesth Essays Res 2014;8:367-71.
15. Werner JG, Castellon-Larios K, Thongrong C, Knudsen BE, Lowery DS, Antor MA, *et al*. Desflurane allows for a faster emergence when compared to sevoflurane without affecting the baseline cognitive recovery time. Front Med (Lausanne) 2015;2:75.
16. Hendrickx JF, Coddens J, Callebaut F, Artico H, Deloof T, Demeyer I, *et al*. Effect of N_2O on sevoflurane vaporiser settings during minimal- and low-flow anesthesia. Anesthesiology 2002;97:400-4.

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